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=> d his

     (FILE 'HOME' ENTERED AT 10:26:03 ON 19 OCT 2005)

     FILE 'EPFULL, FRFULL, GBFULL, PATDPAFULL, PCTFULL, RDISCLOSURE,
     USPATFULL, USPAT2' ENTERED AT 10:26:20 ON 19 OCT 2005
                E GRAHAM B/IN
L1             11 S E10-E11
L2             10 S L1 AND (?STATIN OR HMG? OR VIRUS OR VIRAL OR ANTIVIR?)
L3           8630 S (?STATIN OR HMG?)(L) ((VIRUS OR VIRAL OR ANTIVIR?)(S)(RSV OR
L4          11838 S LOVASTATIN OR SIMVASTATIN OR FLUVASTATIN OR ATORVASTATIN OR P
L5            802 S L4(L)((VIRUS OR VIRAL OR ANTIVIR?)(S)(RSV OR RESPIRTORY OR ?
L6             46 S L5 NOT PY>=2000

     FILE 'MEDLINE' ENTERED AT 10:58:55 ON 19 OCT 2005
L7              4 S L5

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 11:01:27 ON 19 OCT 2005

     FILE 'EMBASE, BIOSIS' ENTERED AT 11:01:43 ON 19 OCT 2005
L8             11 S L7
L9              7 DUP REM L8 (4 DUPLICATES REMOVED)
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=> d ibib 1-10

L2 ANSWER 1 OF 10 EPFULL COPYRIGHT 2005 EPO/FIZ KA on STN

ACCESSION NUMBER: 2003:60963 EPFULL
UPDATE DATE PUBLICAT.: 20050518
DATA UPDATE DATE: 20050518
DATA UPDATE WEEK: 200520
TITLE (ENGLISH): METHOD OF USING PROSTACYCLIN TO TREAT RESPIRATORY SYNCYTIAL **VIRUS** INFECTIONS
TITLE (FRENCH): PROCEDES D'UTILISATION DE LA PROSTACYCLINE POUR TRAITER DES INFECTIONS VIRALES RESPIRATOIRES SYNCYTIALES
INVENTOR(S): PEEBLES, Ray Stokes, Jr.,, 3816 Hobbs Road, Nashville, TN 37215, US; HASHIMOTO, Koichi,, 63 Azuma Fukuhara Fukuyama, Kohriyama, Fukushima 9638061, JP; **GRAHAM, Barney S.,, 301 Pure Spring Crescent, Rockville, MD 20850, US**
PATENT APPLICANT(S): VANDERBILT UNIVERSITY, 305 Kirkland Hall, Nashville, TN 37240, US
PATENT APPL. NUMBER: 554283
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
LANGUAGE OF PROCEDURE: English
LANGUAGE OF TITLE: English; French
DOCUMENT TYPE: Patent
PATENT INFO TYPE: WOA2 International application published without search report
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003103612	A2	20031218

DESIGNATED STATES: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LU MC NL PT RO SE SI SK TR
APPLICATION INFO.: EP 2003-751740 A 20030317
WO 2003-US8280 A 20030317
PRIORITY INFO.: US 2002-364395P P 20020315
US 2003-389295 A 20030314

L2 ANSWER 2 OF 10 EPFULL COPYRIGHT 2005 EPO/FIZ KA on STN

ACCESSION NUMBER: 1999:46142 EPFULL
UPDATE DATE PUBLICAT.: 20050113
DATA UPDATE DATE: 20050112
DATA UPDATE WEEK: 200502
TITLE (ENGLISH): INHIBITION OF **VIRAL** INFECTION AND SPREAD WITH **VIRAL** AND RHOA-DERIVED PEPTIDES
TITLE (FRENCH): INHIBITION DE L'INFECTION ET DE LA PROPAGATION VIRALES AU MOYEN DE PEPTIDES VIRAUX ET DERIVES DE RhoA
TITLE (GERMAN): VERMEIDUNG VIRALER INFEKTION UND VERBREITUNG MITTELS PEPTIDEN, DIE VON VIREN UND VON RHOA ABSTAMMEN
INVENTOR(S): **GRAHAM, Barney, Scott, 2414 Barton Avenue, Nashville, TN 37212, US**; PASTEY, Manoj, 730 Shadowood Drive, Nashville, TN 37205, US
PATENT APPLICANT(S): Vanderbilt University, Office of Technology Transfer, 405 Kirkland Hall, Nashville, TN 37219, US
PATENT APPL. NUMBER: 2906450
AGENT: Dehmel, Albrecht, Dr., et al, Dehmel & Bettenhausen Patentanwaelte, Herzogspitalstrasse 11, 80331 Muenchen, DE
AGENT NUMBER: 77812
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
LANGUAGE OF PROCEDURE: English
LANGUAGE OF TITLE: German; English; French
DOCUMENT TYPE: Patent
PATENT INFO TYPE: EPA2 Application published without search report
PATENT INFORMATION:
PATENT INFORMATION:

PATENT INFORMATION:

NUMBER	KIND	DATE
NUMBER	KIND	DATE
NUMBER	KIND	DATE
EP 1082428	A2	20010314
EP 1082428	A3	20000217
WO 9962932		19991209

DESIGNATED STATES: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION INFO.:			
	EP 1999-927182	A	19990603
	WO 1999-US12338	A	19990603
PRIORITY INFO.:	US 1998-87955P	P	19980604
	US 1998-129565	A	19980805

L2 ANSWER 3 OF 10 PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER: 2003103612 PCTFULL ED 20040102 EW 200351

TITLE (ENGLISH): METHOD OF USING PROSTACYCLIN TO TREAT RESPIRATORY SYNCYTIAL **VIRUS** INFECTIONS

TITLE (FRENCH): PROCEDES D'UTILISATION DE LA PROSTACYCLINE POUR TRAITER DES INFECTIONS VIRALES RESPIRATOIRES SYNCYTIALES

INVENTOR(S): PEEBLES, Ray Stokes, Jr.,, 3816 Hobbs Road, Nashville, TN 37215, US;
HASHIMOTO, Koichi,, 63 Azuma Fukuhara Fukuyama, Kohriyama, Fukushima 9638061, JP;
GRAHAM, Barney S.,, 301 Pure Spring Crescent, Rockville, MD 20850, US

PATENT ASSIGNEE(S): VANDERBILT UNIVERSITY, 305 Kirkland Hall, Nashville, TN 37240, US [US, US]

AGENT: SHOUSE, Emily, A.$, Waddey & Patterson, 414 Union Street, Suite 2020, Bank of America Plaza, Nashville, TN 37219$, US

LANGUAGE OF FILING: English

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003103612	A2	20031218

DESIGNATED STATES

W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
RW (ARIPO):	GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
RW (EAPO):	AM AZ BY KG KZ MD RU TJ TM
RW (EPO):	AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR
RW (OAPI):	BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:			
	WO 2003-US8280	A	20030317
PRIORITY INFO.:	US 2002-60/364,395		20020315
	US 2003-60/364,395		20030314

L2 ANSWER 4 OF 10 PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER: 1999062932 PCTFULL ED 20020515

TITLE (ENGLISH): INHIBITION OF **VIRAL** INFECTION AND SPREAD WITH **VIRAL** AND RhoA-DERIVED PEPTIDES

TITLE (FRENCH): INHIBITION DE L'INFECTION ET DE LA PROPAGATION VIRALES AU MOYEN DE PEPTIDES VIRAUX ET DERIVES DE RhoA

INVENTOR(S): **GRAHAM, Barney, Scott;**
PASTEY, Manoj

PATENT ASSIGNEE(S): VANDERBILT UNIVERSITY

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9962932	A2	19991209

DESIGNATED STATES
W: AU CA JP AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1999-US12338 A 19990603
PRIORITY INFO.: US 1998-60/087,955 19980604
US 1998-09/129,565 19980805

L2 ANSWER 5 OF 10 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1996011019 PCTFULL ED 20020514
TITLE (ENGLISH): INTERLEUKIN-12 AS AN ADJUVANT FOR PARAMYXOVIRIDAE VACCINES
TITLE (FRENCH): INTERLEUKINE-12 UTILISEE EN TANT QU'ADJUVANT POUR VACCINS CONTRE LES PARAMYXOVIRIDAE
INVENTOR(S): **GRAHAM, Barney, S.**;
TANG, Yi-Wei
PATENT ASSIGNEE(S): VANDERBILT UNIVERSITY
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9611019	A1	19960418

DESIGNATED STATES
W: AU CA JP MX AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.: WO 1995-US12656 A 19951002
PRIORITY INFO.: US 1994-8/318,480 19941005

L2 ANSWER 6 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2005:260868 USPATFULL
TITLE: Inhibition of **viral** infection and spread with **viral** and RhoA-derived peptides
INVENTOR(S): **Graham, Barney S.**, Rockville, MD, UNITED STATES
Patsey, Manoj, Corvallis, OR, UNITED STATES
PATENT ASSIGNEE(S): Vanderbilt University (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005226889	A1	20051013
APPLICATION INFO.:	US 2004-984377	A1	20041109 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-129565, filed on 5 Aug 1998, GRANTED, Pat. No. US 6814968

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-87955P	19980604 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FULBRIGHT & JAWORSKI L.L.P., 600 CONGRESS AVE., SUITE 2400, AUSTIN, TX, 78701, US
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1-17
NUMBER OF DRAWINGS: 3 Drawing Page(s)
LINE COUNT: 1639

L2 ANSWER 7 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2004:282629 USPATFULL
TITLE: Inhibition of **viral** infection and spread with **viral** and RhoA-derived peptides
INVENTOR(S): **Graham, Barney Scott**, Nashville, TN, United States
Pastey, Manoj, Nashville, TN, United States
PATENT ASSIGNEE(S): Vanderbilt University, Nashville, TN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6814968	B1	20041109
APPLICATION INFO.:	US 1998-129565		19980805 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-87955P	19980604 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Scheiner, Laurie
LEGAL REPRESENTATIVE: Fulbright & Jaworski
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 1651
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 8 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2003:307038 USPATFULL
TITLE: Method of using prostacyclin to treat respiratory syncytial **virus** infections
INVENTOR(S): Peebles, Ray Stokes, JR., Nashville, TN, UNITED STATES
Hashimoto, Koichi, Fukushima, JAPAN
Graham, Barney S., Rockville, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003216474	A1	20031120
APPLICATION INFO.:	US 2003-389295	A1	20030314 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-364395P	20020315 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WADDEY & PATTERSON, 414 UNION STREET, SUITE 2020, BANK OF AMERICA PLAZA, NASHVILLE, TN, 37219
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 1178
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 9 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2002:259368 USPATFULL
TITLE: Method of inhibiting **viral** infection using **HMG**-COA reductase inhibitors and isoprenylation inhibitors
INVENTOR(S): **Graham, Barney Scott**, Rockville, MD, UNITED STATES
Gower, Tara L., Nashville, TN, UNITED STATES
Pastey, Manoj K., Silver Spring, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002142940	A1	20021003
APPLICATION INFO.:	US 2001-981682	A1	20011016 (9)

Instant Application

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-241247P	20001017 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FULBRIGHT & JAWORSKI L.L.P., A REGISTERED LIMITED PARTNERSHIP, SUITE 2400, 600 CONGRESS AVENUE, AUSTIN,

TX, 78701
NUMBER OF CLAIMS: 51
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 1297
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 10 OF 10 USPATFULL on STN
ACCESSION NUMBER: 2000:70822 USPATFULL
TITLE: Interleukin-12 as an adjuvant for paramyxoviridae vaccines
INVENTOR(S): **Graham, Barney S.**, Nashville, TN, United States
Tang, Yi-Wei, Nashville, TN, United States
PATENT ASSIGNEE(S): Vanderbilt University, Nashville, TN, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6071893		20000606
APPLICATION INFO.:	US 1997-980160		19971126 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-318480, filed on 5 Oct 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hauda, Karen M.
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 793
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L7 ANSWER 1 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2001647015 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11699619
TITLE: Spontaneous reports on drug-induced pancreatitis in Denmark from 1968 to 1999.
AUTHOR: Andersen V; Sonne J; Andersen M
CORPORATE SOURCE: Medical Department, Viborg County Hospital, Denmark.. vandersen@dadlnet.dk
SOURCE: European journal of clinical pharmacology, (2001 Sep) 57 (6-7) 517-21.
Journal code: 1256165. ISSN: 0031-6970.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20011112
Last Updated on STN: 20020429
Entered Medline: 20020426

AB OBJECTIVES: To present an update on drug-induced pancreatitis reported to the Danish Committee on Adverse Drug Reactions. DESIGN: Retrospective study of spontaneous case reports to the Danish reporting system on adverse drug reactions. METHODS: All cases of suspected drug-induced pancreatitis reported to the Danish Committee on Adverse Drug Reactions from 1968 to 1999 were analysed. Three cases were excluded leaving 47 cases for analysis. RESULTS: Drug-induced pancreatitis made up 0. 1% of all the reports to the committee from 1968 to 1999. The proportion seemed to increase and was 0.3% during the last 8 years. The 47 cases corresponded to 0.1% of the number of patients discharged due to pancreatic disease (without cancers) per year in Denmark. Serious courses were frequent as indicated by death and hospitalisation being reported in 4 (9%) and 32 (68%) cases, respectively. Death occurred after valproate (two cases), clomipramine (one case) and azathioprine (one case). Definite relationship was stated for mesalazine (three cases), azathioprine (two cases) and **simvastatin** (one case) on the basis of re-challenge. A possible or probable causality was considered for a further 30 drugs including 5-acetylsalicylic acid agents, angiotensin-converting enzyme inhibitors, estrogen preparations, didanosine, valproate, codeine, **antiviral** agents used in acquired immunodeficiency syndrome therapy, various lipid-reducing agents, interferon, paracetamol, griseofulvin, ticlopine, allopurinol, lithium and the MMR (**measles**" mumps/rubella) vaccination. CONCLUSION: Drug-induced pancreatitis is rarely reported. The incidence may be increasing and the course is often serious. This is the first report on definite **simvastatin**-induced pancreatitis. Further studies on the pancreotoxic potential of drugs are warranted.

L7 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2001504507 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11257039
TITLE: Antiviral activity of lovastatin against respiratory syncytial virus in vivo and in vitro.
AUTHOR: Gower T L; Graham B S
CORPORATE SOURCE: Department of Microbiology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.
CONTRACT NUMBER: RO1-AI-33933 (NIAID)
SOURCE: Antimicrobial agents and chemotherapy, (2001 Apr) 45 (4) 1231-7.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010917

Last Updated on STN: 20010917
Entered Medline: 20010913

AB Respiratory syncytial **virus** (**RSV**) is an important human pathogen that can cause severe and life-threatening respiratory infections in infants and immunocompromised adults. We have recently shown that the **RSV** F glycoprotein, which mediates **viral** fusion, binds to RhoA. One of the steps in RhoA activation involves isoprenylation at the carboxy terminus of the protein by geranylgeranyltransferase. This modification allows RhoA to be attached to phosphatidyl serine on the inner leaflet of the plasma membrane. Treatment of mice with **lovastatin**, a drug that inhibits prenylation pathways in the cell by directly inhibiting hydroxymethylglutaryl coenzyme A reductase, diminishes **RSV** but not vaccinia **virus** replication when administered up to 24 h after **RSV** infection and decreases **virus**-induced weight loss and illness in mice. The inhibition of replication is not likely due to the inhibition of cholesterol biosynthesis, since gemfibrozil, another cholesterol-lowering agent, did not affect virus replication and serum cholesterol levels were not significantly lowered by **lovastatin** within the time frame of the experiment. **Lovastatin** also reduces cell-to-cell fusion in cell culture and eliminates RSV replication in HEp-2 cells. These data indicate that **lovastatin**, more specific isoprenylation inhibitors, or other pharmacological approaches for preventing RhoA membrane localization should be considered for evaluation as a preventive **antiviral** therapy for selected groups of patients at high risk for severe **RSV** disease, such as the institutionalized elderly and bone marrow or lung transplant recipients.

L7 ANSWER 3 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2001326270 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11336544
TITLE: RhoA is activated during respiratory syncytial virus infection.
AUTHOR: Gower T L; Peeples M E; Collins P L; Graham B S
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.
CONTRACT NUMBER: RO1-AI-33933 (NIAID)
SOURCE: Virology, (2001 May 10) 283 (2) 188-96.
Journal code: 0110674. ISSN: 0042-6822.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607

AB Respiratory syncytial **virus** (**RSV**) is an important human pathogen that can cause severe and life-threatening respiratory infections in infants and immunocompromised adults. We have recently shown the **RSV** F glycoprotein, which mediates **viral** fusion and entry, interacts with the cellular protein RhoA in two-hybrid and in vitro binding assays. Whether this interaction occurs in living cells remains an open question. However, because RhoA signaling is associated with many cellular functions relevant to RSV pathogenesis such as actin cytoskeleton organization, expression of proinflammatory cytokines, and smooth muscle contraction, we asked whether RhoA activation occurred during RSV infection of HEp-2 cells. We found that the amount of isoprenylated and membrane-bound RhoA in RSV-infected cultures was increased. Further evidence of RhoA activation was demonstrated by downstream signaling activity mediated by RhoA. There was an increase in p130(cas) phosphorylation during RSV infection, which was prevented by Y-27632, a specific inhibitor of Rho kinase, or **lovastatin**, an HMG-CoA reductase inhibitor that reduces the synthesis of groups needed for isoprenylation. In addition, RSV infection of HEp-2 cells resulted in an increase in the formation of actin stress fibers. Pretreatment of HEp-2 cells with Clostridium botulinum C3 exotoxin, an enzyme that

specifically ADP-ribosylates and inactivates RhoA, prevented RSV-induced stress fiber formation. These observations indicate that RhoA and subsequent downstream signaling events are activated during RSV infection, which has implications for RSV pathogenesis.

L7 ANSWER 4 OF 4 MEDLINE on STN
ACCESSION NUMBER: 1998177164 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9508769
TITLE: Cholesterol is required for surface transport of influenza virus hemagglutinin.
AUTHOR: Keller P; Simons K
CORPORATE SOURCE: European Molecular Biology Laboratory, Cell Biology Programme, D-69012 Heidelberg, Germany.
SOURCE: Journal of cell biology, (1998 Mar 23) 140 (6) 1357-67. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980430
Last Updated on STN: 19980430
Entered Medline: 19980420

AB Transport from the TGN to the basolateral surface involves a rab/N-ethylmaleimide-sensitive fusion protein (NSF)/soluble NSF attachment protein (SNAP)/SNAP receptor (SNARE) mechanism. Apical transport instead is thought to be mediated by detergent-insoluble sphingolipid-cholesterol rafts. By reducing the cholesterol level of living cells by 60-70% with **lovastatin** and methyl-beta-cyclodextrin, we show that the TGN-to-surface transport of the apical marker protein **influenza virus** hemagglutinin was slowed down, whereas the transport of the basolateral marker vesicular stomatitis **virus** glycoprotein as well as the ER-to-Golgi transport of both membrane proteins was not affected. Reduction of transport of hemagglutinin was accompanied by increased solubility in the detergent Triton X-100 and by significant missorting of hemagglutinin to the basolateral membrane. In addition, depletion of cellular cholesterol by **lovastatin** and methyl-beta-cyclodextrin led to missorting of the apical secretory glycoprotein gp-80, suggesting that gp-80 uses a raft-dependent mechanism for apical sorting. Our data provide for the first time direct evidence for the functional significance of cholesterol in the sorting of apical membrane proteins as well as of apically secreted glycoproteins.

L19 ANSWER 7 OF 40 MEDLINE on STN
ACCESSION NUMBER: 96367681 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8771795
TITLE: Selection and evolution of high-affinity human anti-viral antibodies.
AUTHOR: Barbas C F 3rd; Burton D R
CORPORATE SOURCE: Department of Molecular Biology, Scripps Research Institute, La Jolla, CA 92037, USA.
SOURCE: Trends in biotechnology, (1996 Jul) 14 (7) 230-4. Ref: 26
Journal code: 8310903. ISSN: 0167-7799.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Biotechnology; AIDS
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961106
Last Updated on STN: 19970203
Entered Medline: 19961024

AB High-affinity human anti-**viral** antibodies [e.g. for human immunodeficiency **virus** type 1 (**HIV**-1), respiratory syncytial **virus** (**RSV**) and herpes simplex **virus** (HSV)] can be selected from immune phage-display libraries using a variety of strategies. A small subset of these antibodies show potent neutralization in vitro and anti-viral efficacy in vivo in animal models. The affinities of such antibodies arising from secondary or higher order immune responses can be improved using "CDR walking'. Sequential and parallel optimization variants of this strategy have been used to improve the affinity of a prototype anti-HIV-1 antibody 420-fold. Ultra-high-affinity human antibodies could constitute a new class of useful anti-viral reagents.

L19 ANSWER 19 OF 40 MEDLINE on STN
ACCESSION NUMBER: 94021160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8414800
TITLE: Respiratory syncytial virus illnesses in human immunodeficiency virus- and noninfected children.
AUTHOR: King J C Jr; Burke A R; Clemens J D; Nair P; Farley J J; Vink P E; Batlas S R; Rao M; Johnson J P
CORPORATE SOURCE: Department of Pediatrics, University of Maryland School of Medicine, Baltimore 21201.
CONTRACT NUMBER: RO1 AI29816 (NIAID)
SOURCE: Pediatric infectious disease journal, (1993 Sep) 12 (9) 733-9.
Journal code: 8701858. ISSN: 0891-3668.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931123

AB Respiratory syncytial **virus** (**RSV**) lower respiratory tract and febrile upper respiratory tract illnesses were prospectively assessed in cohorts of 83 infants born to human immunodeficiency **virus** (**HIV**)- and of 48 infants born to non-**HIV**-infected mothers. Of the infants born to HIV-infected mothers, 18 were themselves infected with HIV, 26 were indeterminant and 39 were free from HIV. Ten RSV illnesses occurred in 8 HIV-infected, 2 illnesses in 2 indeterminant and 17 illnesses occurred in 17 non-HIV-infected children. RSV shedding was prolonged in HIV class P2- vs. non-HIV-infected children, at medians of 30 days (range, 1 to 199 days) and 6 days (range, 1 to 21 days), respectively ($P = 0.02$). Ribavirin and intravenous immunoglobulin failed to eradicate RSV from one child who shed virus for 199 days. Wheezing occurred in 1 of 4 vs. 9 of 10 episodes of lower respiratory tract illness in HIV-infected and non-HIV-infected children, respectively ($P = 0.04$). No differences were noted in duration of illness, temperature, respiratory rate or oxygen saturation between HIV- and non-HIV-infected children. Infection control and public health concerns regarding prolonged shedding of RSV in HIV-infected children must be recognized.

ACCESSION NUMBER: 1998370873 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9707376
TITLE: RD6-2198, a novel betain-type fluoroalkylated oligomer, inhibits the replications of human immunodeficiency virus type 1 and other enveloped viruses.
AUTHOR: Fujiwara M; Ashida N; Okamoto M; Mizuta T; Ide T; Hanasaki Y; Katsuura K; Sawada H; Shigeta S; Konno K; Yokota T; Baba M
CORPORATE SOURCE: Rational Drug Design Laboratories, Matsukawamachi, Fukushima, Japan.. fuji@rdl.co.jp
SOURCE: Antiviral research, (1998 May) 38 (2) 141-9.
Journal code: 8109699. ISSN: 0166-3542.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981016
AB We have examined a novel betain-type fluoroalkylated oligomer, RD6-2198, for its inhibitory effects on the replication of human immunodeficiency **virus** type 1 (**HIV**-1) and other enveloped **viruses**, including herpes simplex **virus** types 1 and 2 (HSV-1 and HSV-2, respectively) and respiratory syncytial **virus** (**RSV**) in cell cultures. We have found that the compound is a potent and selective inhibitor of these viruses. RD6-2198 inhibited the replication of HIV-1IIIB at a concentration of 0.85 microg/ml with a selectivity index greater than 59 in MT-4 cells. Furthermore, its 50% effective concentration (EC50) values for HSV-1, HSV-2 and RSV, were 0.51, 0.94 and 3.0 microg/ml, respectively. We found that the RD6-2198 suppressed the gp120-CD4 interaction (as monitored by an enzyme-linked immunosorbent assay (ELISA) method). RD6-2198 also inhibited the binding of anti-gp120 monoclonal antibody to gp120 expressed on MOLT-4/IIIB cells (MOLT-4 cells chronically infected with HIV-1IIIB). However, the compound did not inhibit the interaction of anti-CD4 antibody with CD4. These results suggest that RD6-2198 interacts with the viral envelope glycoprotein and thereby inhibits the viral adsorption process. In addition, RD6-2198 was also found to suppress the proliferation of MOLT-4/IIIB cells. When applied topically, RD6-2198 at a concentration of 10 mg/ml completely protected mice from an intravaginal HSV-2 infection.

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AB The proteolytic cleavage sites of the human immunodeficiency **virus** type 1 (**HIV**-1) envelope glycoprotein precursor gp160 and the fusion protein of respiratory syncytial **virus** (**RSV**) show a sequence homology. To study this homology two synthetic peptides corresponding to HIV-1-env-gp160-aa 507-518 (KAKRRVVQREKR) and RSV-F2-aa 130-136 (SKKRKRR) were synthesized. Human serum samples from HIV-positive or RSV-positive collections recognized the appropriate peptide in 90.6 or 37.2% respectively. No cross-reactivity towards the nonhomologous peptide could be monitored in both serum collections. In contrast, antipeptide antibodies raised against both peptides demonstrate a high degree of cross-reactivity. These data indicate that the high specificity of the virus-induced antibodies may be a result of strong conformational restrictions at the proteolytic cleavage site of both proteins. Moreover, these observations are important for diagnostic purposes. Synthetic peptides are a valuable tool for HIV antibody screening. Our data provide information concerning the specificity of antigen-antibody interaction on a highly immunogenic HIV-1 epitope.